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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/509,323	05/31/2005	Hiroaki Matsuno	259979US0PCT	7538
22850	7590	06/02/2006		
OBLON, SPIVAK, MCCLELLAND, MAIER & NEUSTADT, P.C. 1940 DUKE STREET ALEXANDRIA, VA 22314			EXAMINER CHOI, FRANK I	
			ART UNIT	PAPER NUMBER

1616

DATE MAILED: 06/02/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/509,323	MATSUNO ET AL.	
	Examiner	Art Unit	
	Frank I. Choi	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 07 March 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-4 and 10-14 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☐ Claim(s) _____ is/are rejected.
- 7) ☒ Claim(s) 1-4 and 10-14 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 07 March 2006 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Drawings

The drawings filed 3/7/2006 are objected to because Figures 1,2,5-14 do not have sufficient clarity. Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as “amended.” If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either “Replacement Sheet” or “New Sheet” pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Examiner notes that Applicant has filed color drawings or photographs, however, Color photographs and color drawings are not accepted unless a petition filed under 37 CFR 1.84(a)(2) is granted. Any such petition must be accompanied by the appropriate fee set forth in 37 CFR 1.17(h), three sets of color drawings or color photographs, as appropriate, and, unless already present, an amendment to include the following language as the first paragraph of the brief description of the drawings section of the specification:

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The patent or application file contains at least one drawing executed in color. Copies of this patent or patent application publication with color drawing(s) will be provided by the Office upon request and payment of the necessary fee.

Color photographs will be accepted if the conditions for accepting color drawings and black and white photographs have been satisfied. See 37 CFR 1.84(b)(2).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4,10,12 are rejected under 35 U.S.C. 102(b) as being anticipated by Miyazaki et al..

Miyazaki et al. expressly discloses cross-linked hyaluronan gel having a molecular weight of 1.6×10^6 containing doxycycline and magnesium chloride in which the hyaluronan was pre-heated to 60 degree Celsius which exhibits slower release of the antibiotic versus molecular weights of 0.8 and 0.1×10^6 (Page 337, Abstract, Pages 344,345, Figure 9). It is inherent that that the composition has auto-cross linked inner esters. See US 6,251,876, Column 4, lines 25-65)(inner esters are formed by activation with alkaline or alkaline metal earth salts and heating).

Examiner has duly considered Applicant's arguments but deems them moot in light of the new grounds of rejection herein. With respect to the Declaration (3/7/2006), secondary considerations are not applicable to rejections under 102(b). To the extent that auto-crosslinking may fall under the aspect of obviousness rather than anticipation, contrary to the declaration, in

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view of the express disclosure of Miyazaki et al., it is not unexpected that molecular weight greater than 800,000 would exhibit a slower or extended rate of release of the antibiotic.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-4, 10-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bellini et al. (US Pat. 6,251,876) in view of Collins et al. (US Pat. 6,096,728), Balazs (US Pat. 4,141,973) and Miyazaki et al..

Bellini et al. disclose an autocross-linked hyaluronic acid (HA) containing intra- and inter chain ester bonds where autocross-linked HA can be synthesized from HA having a molecular weight in the range from 50 kDa to 5,000 kDa that is used to treat arthropathies (Column 3, lines 20-38). It is disclosed that the autocross-linked HA can also contain external esters by cross linking with mono or polyvalent alcohol (Column 5, lines 8-23). It is disclosed that the composition can include an antibiotic (Column 4, lines 6-9, Claim 4). It is disclosed that autocross-linked hyaluronic acid (HA) has gel-like properties in aqueous media (Column 3, lines 56-59).

Collins et al. disclose the combination of a drug substance and cross-linked hyaluronan gels and that the drug can be used to treat inflammatory conditions of a joint such as gentamicin, vancomycin and structurally related antimicrobials (Column 7, lines 10-19, Column 28, lines 31-38, Column 32, lines 34-50).

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Balazs discloses a non-inflammatory ultrapure hyaluronic acid fraction having an average molecular weight greater than about 750,000, preferably greater than about 1,200,000 (Column 4, lines 16-49).

Miyazaki et al. discloses cross-linked hyaluronan gel having a molecular weight of 1.6×10^6 containing doxycycline and magnesium chloride in which the hyaluronan was pre-heated to 60 degree Celsius which exhibits slower release of the antibiotic versus molecular weights of 0.8 and 0.1×10^6 (Page 337, Abstract, Pages 344,345, Figure 9).

The prior art discloses gel compositions containing auto cross-linked HA having ester linkages which can contain antibiotics which are used to treat arthropathies. The difference between the prior art and the claimed invention is that the prior art does not expressly disclose the use of cross-linked HA having a molecular weight greater than 800,000. However, the prior art amply suggests the same as the prior art discloses that auto cross-linked HA can be synthesized from HA have a molecular weight range from range from 50 kDa to 5,000 kDa; a purified HA having a molecular weight at least about 750, 000, preferably 1,200,000, is disclosed that is non-inflammatory; a composition containing antibiotic and cross-linked HA having a molecular weight of 1.6×10^6 is disclosed in the art which exhibits slower release versus 0.8 and 0.1×10^6 ; and a gel containing cross-linked HA and antibiotic, such as gentamicin and vancomycin, for anti-inflammatory treatment of joints is disclosed. As such, it would have been well within the skill of one of ordinary skill in the art to modify the prior art as above with the expectation that molecular weights of cross-linked HA greater than 800,000 would extend release of the antibiotic greater than molecular weights below 800,000 and that the non-inflammatory purified HA having a molecular weight at least about 750,000 would be

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especially suitable for preparation of autocross linked HA which is used in combination with antibiotics, such as gentamicin and vancomycin, to treat inflammatory joint conditions. In the case where the claimed ranges “overlap or lie inside ranges disclosed by the prior art” a prima facie case of obviousness exists. See *In re Wertheim*, 541 F.2d 257, 191 USPQ 90 (CCPA 1976); *In re Woodruff*, 919 F.2d 1575, 16 USPQ2d 1934 (Fed. Cir. 1990); *In re Geisler*, 116 F.3d 1465, 1469-71, 43 USPQ2d 1362, 1365-66 (Fed. Cir. 1997).

Examiner has duly considered Applicant's arguments but deems them moot in light of the new grounds of rejection herein. In view of the disclosure of Miyazaki et al., the Declaration (3/7/2006) does not over come the prima facie case of obviousness as it is not unexpected that molecular weights of cross-linked HA greater than 800,000 would exhibit a slower or extended rate of release of the antibiotic versus molecular weight less than 800,000.

Therefore, the claimed invention, as a whole, would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, because every element of the invention has been collectively taught by the combined teachings of the references.

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Conclusion

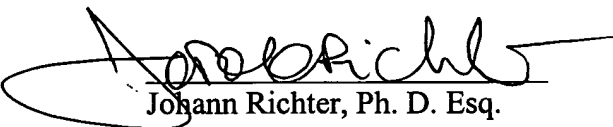
A facsimile center has been established in Technology Center 1600. The hours of operation are Monday through Friday, 8:45 AM to 4:45 PM. The telecopier number for accessing the facsimile machine is 571-273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Choi whose telephone number is (571)272-0610. Examiner maintains a flexible schedule. However, Examiner may generally be reached Monday-Friday, 8:00 am – 5:30 pm (EST), except the first Friday of the each biweek which is Examiner's normally scheduled day off.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's Supervisor, Mr. Johann Richter, can be reached at (571)272-0646. Additionally, Technology Center 1600's Receptionist and Customer Service can be reached at (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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May 21, 2006


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